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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,444	08/15/2001	Koichi Ito	0425-0847P	9635

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EXAMINER
KIFLE, BRUCK

ART UNIT	PAPER NUMBER
1624	5

DATE MAILED: 02/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/913,444	Ito et al.
Examiner	**Art Unit**
Bruck Kifle	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 15, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-31* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Claim Rejections - 35 USC § 112

Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) Applicants are reminded of the proper format for presenting claims. A claim should end in a period and should have only one period. See for example claims 1, 13 and 15.

ii) The term "heterodiazinon" is confusing. Deletion is suggested because the term "compound" along with the structural formula and the definitions of the variables fully describe the compound being claimed.

iii) The term "substituted" without saying which substituents are intended is indefinite. One skilled in the art cannot say which substituents are permitted and which ones are not.

iv) The term "heteroaryl" is indefinite because it is not known how many atoms are present, how many and what kind of heteroatoms are involved, what size ring is intended and how many rings are present.

v) The group "optionally substituted amide group" is unclear as to how the group is bonded to the rest of the molecule (carbonyl or nitrogen) and what the rest of this group looks like.

vi) The term "cycloalkyl" and "adamantyl" are both present in the claims. However, cycloalkyl embraces adamantyl. Deletion is suggested.

vii) It is unclear which diseases are embraced by claims 22 and 23, and which ones are not.

Claims 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for preventing, treating and ameliorating diseases against which non-N-methyl-D-aspartate excitatory amino acid receptor antagonistic action is effective, against which 2-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor antagonistic action is effective, nerve degeneration diseases, demyelinating nerve diseases and the diseases in claim 26.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: The method of use claims are drawn in part to preventing, treating and ameliorating any and all diseases against which non-N-methyl-D-aspartate excitatory amino acid receptor antagonistic action is effective, against which 2-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor antagonistic action is effective, nerve degeneration diseases, demyelinating nerve diseases and the diseases in claim 26.

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated to prevent, treat or ameliorate diseases against which non-N-methyl-D-aspartate excitatory amino acid receptor antagonistic action is effective, against which 2-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor antagonistic action is effective, nerve degeneration

diseases, demyelinating nerve diseases and the diseases in claim 26. There are no known compounds that can treat and prevent all of these disorders. For example, finding agents to be effective against Alzheimer's disease has proven extremely difficult, let alone its prevention. Despite extraordinary efforts with a variety of agents in this area, only two pharmaceuticals have been made to work, both acetylcholinesterase antagonists, a property that these compounds are not disclosed to have. No one has been able to figure out how to prevent AD, which is evidence of the low skill level in this art relative to the difficulty of the task.

3) The predictability or lack thereof in the art: It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop any kind of the disorders recited. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to protect a potential host from the disorders cited, etc. There are no doses present for treatment of the disorders recited and there is no data present for the prophylaxis of these disorders.

6) The breadth of the claims: The claims are drawn to disorders that are not related and whose prevention is unknown.

7) The quantity of experimentation need would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

Claims 27-31 provide for the use of a compound, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 27-31 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Applicant is advised that should claims 15 and 16 be found allowable, claims 17-21 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in

an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Note that the intended use of a pharmaceutical composition does not make it any different, i.e., does not have patentability weight.

Copious amount of compounds have been excluded from claim 1. If these compounds are excluded to avoid prior art rejections, Applicants should point to these compounds in the prior art to the Examiner because, the disclosure of these compounds is material to the examination of the instant application. Thus, a compound that is excluded by proviso renders obvious a compound of the instant claim when, for example, in the instant claims R^{11} represents a C3 chloroalkyl group or a C2 iodoalkyl group or any other homologue, analogue or ring position isomer of the excluded compounds should they be present in the prior art.

It is noted that there are three independent claims (1, 13 and 15). Applicants are requested to point out the difference in scope. Note that compounds, corresponding compositions, a method of use and a process of making that are of the same scope are considered to form a single inventive concept under PCT Rule 13.1, 37 CFR 1.475(d). The claims are being examined according to the scope of claim 1.

Copious amount of art was found that anticipates compounds of the instant claims. Examples are given below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Takamizawa et al. (Chem. Pharm. Bull. (1970), 18(6), 1201-10). The claim reads on the compounds of RN 26734-75-8; 26734-74-7; 26734-75-8; 26734-76-9; 26734-77-0; 25626-39-5 and 25626-41-9. (Reference provided by Applicants).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Gaozza et al. (J. Heterocycl. Chem. (1970), 7(4), 927-30). The claim reads on the compounds of RN 28669-15-0P; 28669-16-1P; 28669-23-0P and 28669-25-2P. (see CAS abstract and structure).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Sicardi et al. (J. Pharm. Sci. (1974), 63(8), 1336-7. The claim reads on the compounds in table 1, page 1336 of the reference. (Reference provided by Applicants).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Somer (Angew. Chem. (1976), 88(13), 449). The claim reads on the compound of RN 59231-02-6P (see CAS abstract and structure).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Westphal et al. (J. Prakt. Che. (1978), 320(3), 452-6). The claim reads on the compounds in the CAS printout (see CAS abstract and structure).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Camparini et al. (J. Heterocycl. Chem. (1978), 15(8), 1271-6). The claim reads on the compounds of RN 60206-70-4P; 60206-72-6P and 60206-74-8P. (see CAS abstract and structure).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is (703) 305-4484.

The fax phone number for this Group is (703) 308-4556 or (703) 305-3592. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

February 7, 2002

Bruck Kifle
Primary Examiner
Art Unit 1624